

EPA Washington DC | November 2018

### Agenda



I. Introduction and meeting objectives (10 min)

II. IVCC role - activities update since last meeting (IVCC) (25 min)

III. EPA Challenges and needs (EPA) (30 min)
Health security approach at local and global level

#### Break

IV. Incentivize innovation in Vector Control product regulatory pathways (IVCC and consultants) (30 min)

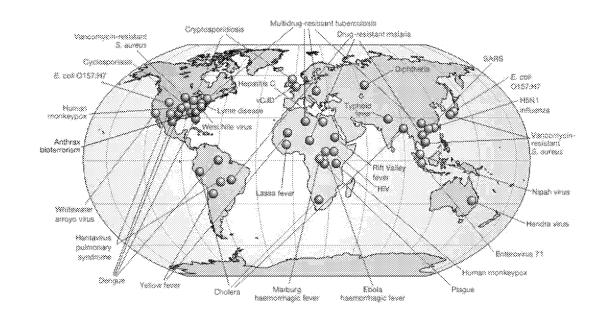
V. Debate and Next steps (All) (50 min)

VI. Conclusion (10 min)

### Purpose of the meeting



- Present the global challenges of vector-borne diseases in a changing environment
- Share views on Biosecurity / health security challenges of arboviruses
- Look at recent changes in the WHO approval process: move from WHOPES to PQ
- Discuss a proposed US response through incentives (data protection or "vector expedited review voucher" – VERV) to encourage new public health use pesticides
- Discuss the benefits/disadvantages of PRIA changes which support the discovery of new public health use pesticides
- Solicit advice on shaping the detailed schemes and on priorities and pathways



Vector borne diseases pose
US national security risk
domestically and internationally

## Summary of the situation



Problem	Solution
Development is expensive	IVCC pays for it?
WHOPES was broken	I2I supports PQ process transformation
Still too many barriers to entry - epidemiology requirements Regulatory process still too slow	Maybe ento correlates and GMP Damascene conversion Find faster process Can EPA/PRIA help?
still too many Disincentives	Data protection Can EPA/PRIA help?
Still not enough incentive to bring insecticide developers to the table or keep them there	VERV , etc. Can EPA/PRIA help?

### IVCC: A Product Development Partnership for Vector Control

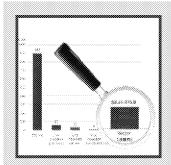


IVCC is a Product Development
Partnership (PDP) investing donor funds in
R&D to overcome barriers to innovation in
vector control.

We facilitate the development and delivery of novel and improved vector control tools and solutions in challenged markets to combat the rapidly growing problem of insecticide resistance



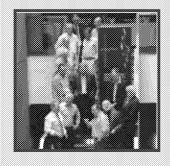




Addressing market challenges



De-risking innovation



Innovator community expert support



Technical project and product management platform



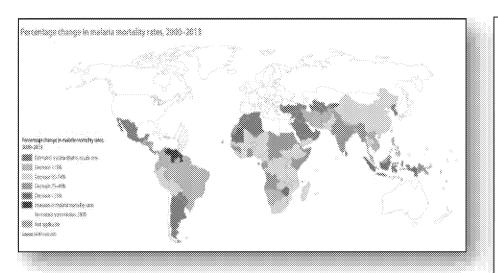
Impact driven



Broad nonpolitical outreach

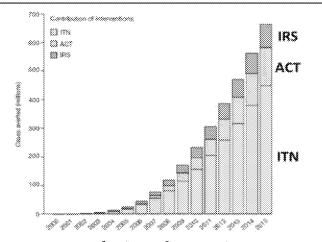
## Vector control using LLINs and IRS accounts for most of the malaria burden reductions achieved since 2000





### Shrinking Malaria Map 2000 – 2015

Malaria deaths globally fell from 839,000 in 2000 to an estimated 446,000 in 2016. The WHO African Region accounted for 91% of all malaria deaths in 2016, followed by the WHO South East Asia Region (6%).



Malaria Atlas Project

Interventions have averted 663 million clinical cases since 2000, with LLINS and IRS making the largest contributor (78% of cases averted).

The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015, S. Bhatt et al, Sep 2015

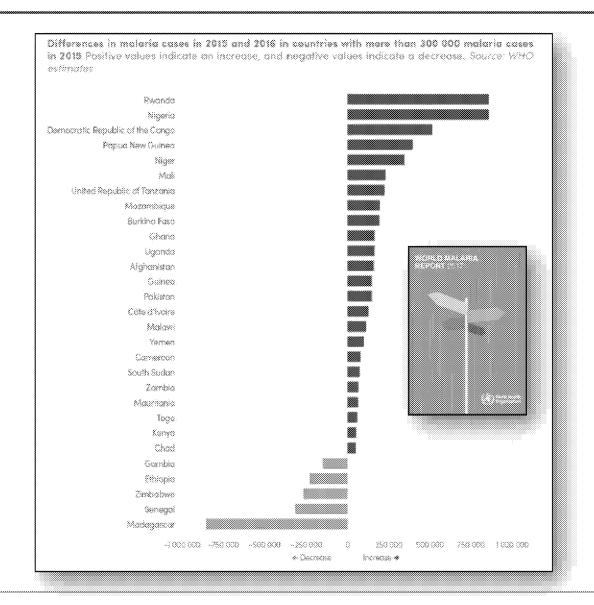


**Dr Tedros Adhanom Shebreyesus** Orector-General World Health Organization

'Last December, we noted a troubling shift in the trajectory of this disease. The data showed that **less than** half of countries with ongoing transmission **were on track** to reach critical targets for reductions in the death and disease caused by malaria. Progress appeared to have stalled. The World malaria report 2017 shows that this worrying trend continues. ...in some countries and regions, we are beginning to see reversals in the gains achieved'

### A public Health concern: the trend is reversing!

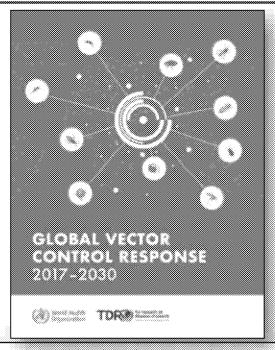






## Global Vector Borne Disease Burden and it is very much on the rise....





#### RISK

80% of the world's population is at risk of one for more vector borne disease.

#### BURDEN

17% of the global burden of communicable diseases is due to vector-borne diseases

### MORTALITY

Over 700 000 deaths are caused by vector barne diseases annually

TABLE 1. GOALS, MILESTONES AND TARGETS FOR THE GLOBAL TECHNICAL STRATEGY FOR MALARIA 2016–2030

#### **VISION – A WORLD FREE OF MALARIA**

GO,	ALS	MILEST	TARGETS	
		2020	2025	2030
	Reduce malaria mortality rates globally compared with 2015	Åt least 40%	At least 75%	At least 90%
2.	Reduce malana case incidence globally compared with 2015	At least 40%	At least 75%	At least 90%
3.	Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
- <b>4.</b>	Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

Figure 2. Overlapping about the solution of more major vector because the solution of a solution of the soluti



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### Global Suitability for Aedes



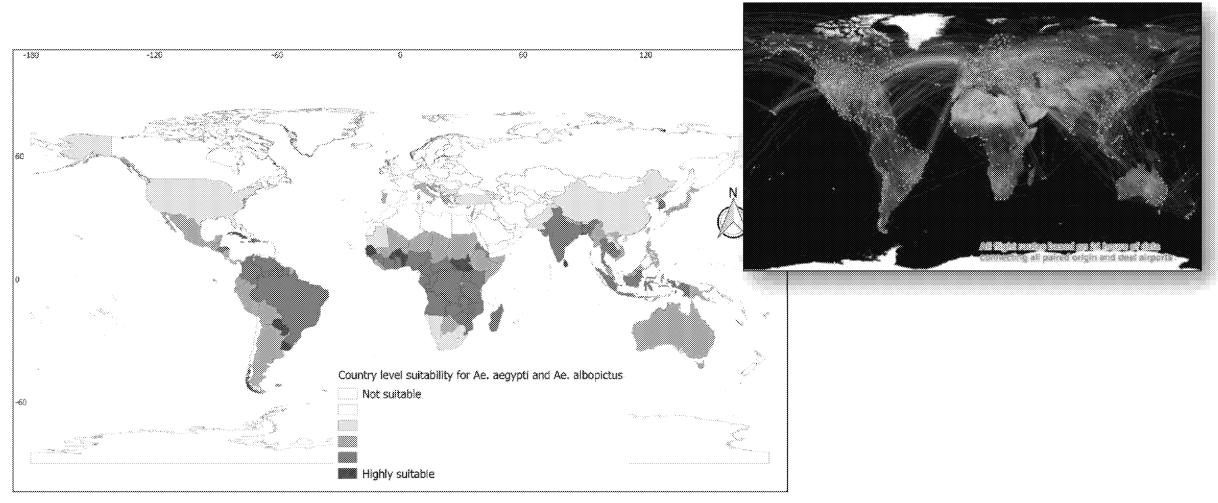


Figure 2. Country-level suitability range for Aedes negypti and/or Aedes albopictus: suitability ranges from 0 (white) to 100% (deep red). The percentage suitability was computed based on all grid cells that manifested suitability levels higher than 0,5.

### Global Disease Risk



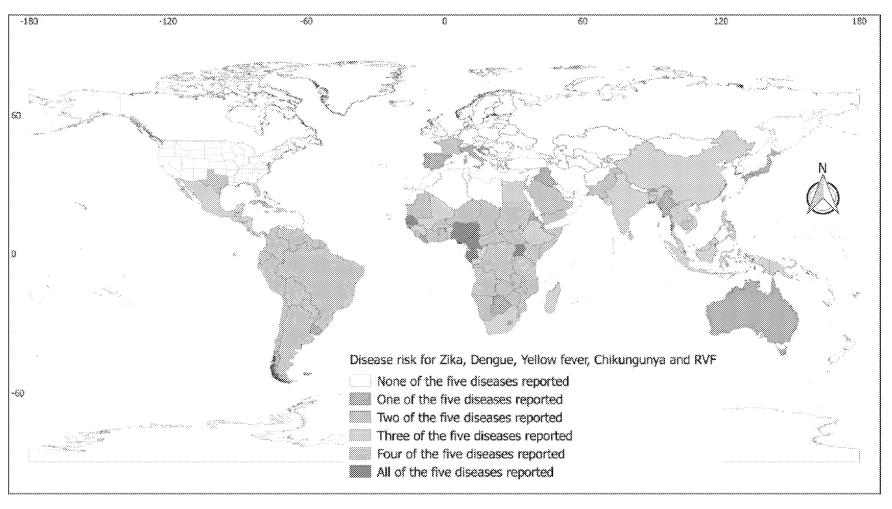


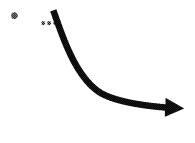
Figure 3. Global country-level occurrences of the selected arboviral diseases. The map depicts the occurrences of selected arboviral diseases from no occurrence, shown in white, to the occurrence of all of the selected arboviral diseases, shown in red.

## IVCC receives a grant from DFAT to capitalizing on the work done for sub-Saharan Africa



### **Enabling innovation:**

- Novel Al development
- Improve data quality
- Formulation platform
- Expert Scientific Advisory Committees
- Application technology
- GLP field testing sites
- Resistance strain testing platform



Creation of a toolbox:
Indoor Residual Sprays
Long-Lasting Insecticide Nets
ATSB
Spatial repellent

\*\*\*

#### Aedes

Chikungunya Dengue fever Lymphatic filariasis Rift Valley fever Yellow fever

#### Culex

Japanese encephalitis Lymphatic filariasis West Nile fever

#### **Recent DFID Funding**

- A Cluster Randomized Controlled Trial to measure the impact of integrated vector management (IVM) on Aedesborne diseases in Malaysia. Industry driven.
- 2. Targeted IRS for Aedes
- 3. <u>VectorWeb</u>: Follow up work to improve this automated surveillance system.

Select most promising projects

Test against local vectors and specific geographies

Address access hurdles

Health Security



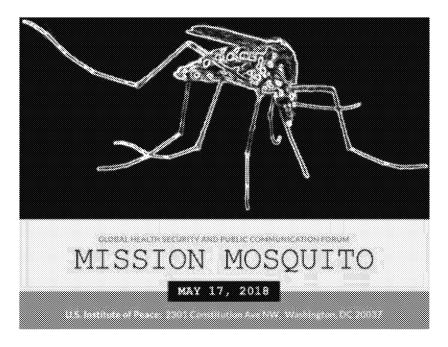


## WHO and GHSA recognize that health risk communication is a pillar of any effective strategy for controlling the spread of Vector borne disease



## Mission Mosquito: Global Health Security and Public Communication Forum

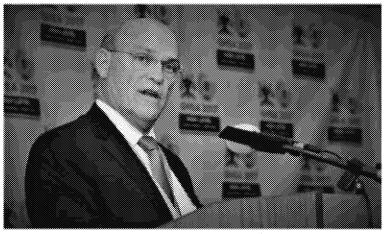
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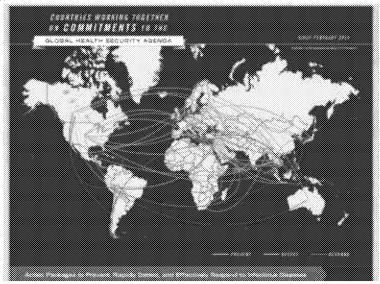


Mosquitoes spread more disease to humans than any other animal. How can we make mosquito control and prevention everyone's mission? The U.S. Department of State is hosting a Public Health Forum as part of efforts to support goals of the Global Health Security Agenda to improve international preparedness to respond to infectious disease threats. The World Health Organization and the Global Health Security Agenda recognize that health risk communication is a piltar of any effective strategy for controlling the spread of vector-borne disease.

missiónmosquito2018.com

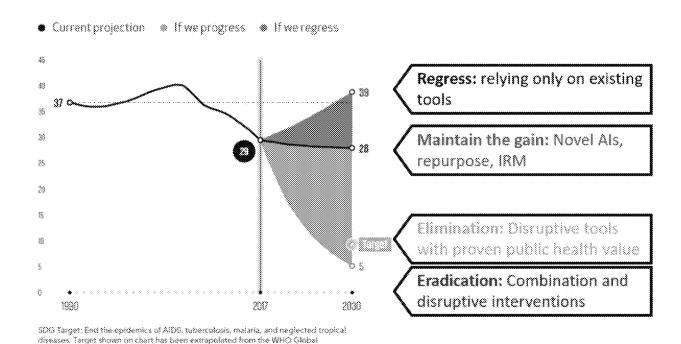
### Strengthening capabilities, fostering partnership top priorities at global health summit



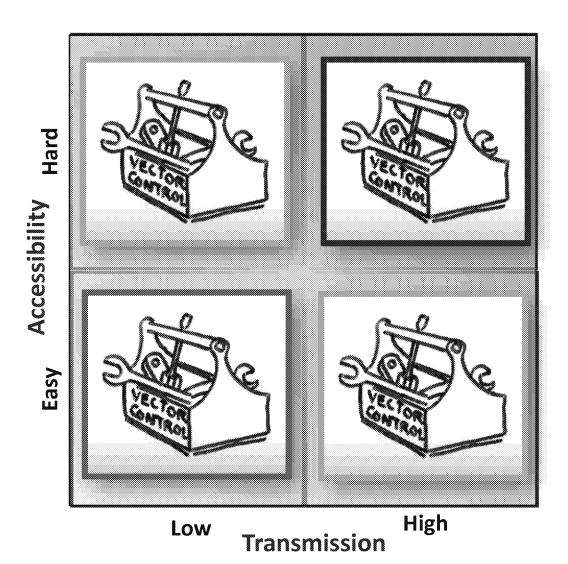


### Creating a toolbox of novel products



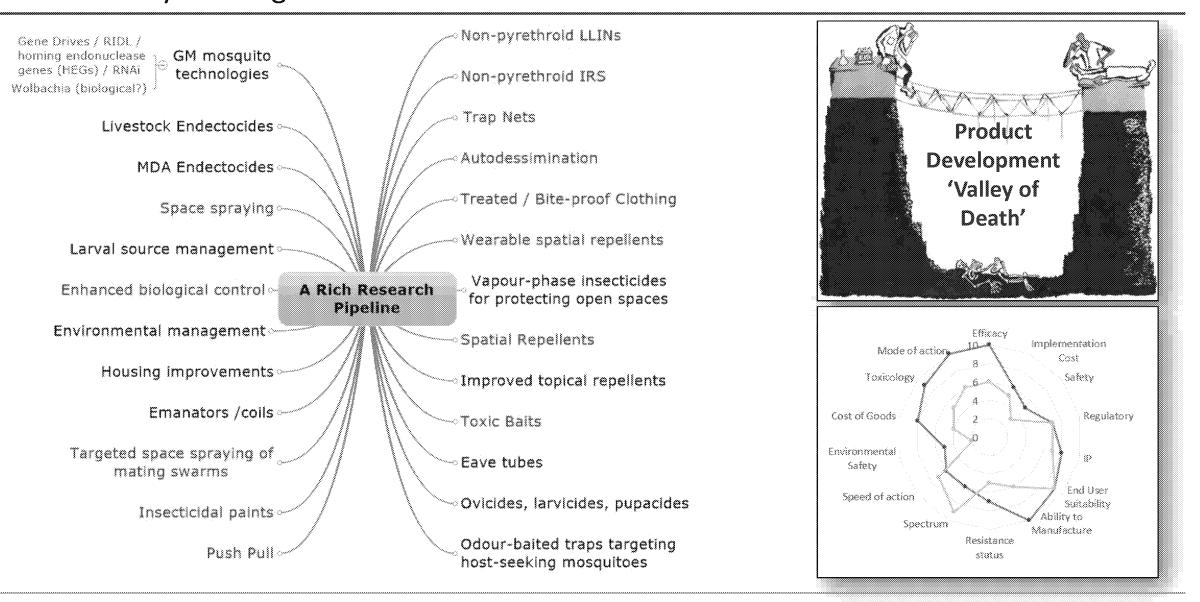


Technical Strategy target of reducing incidence by 90 percent.



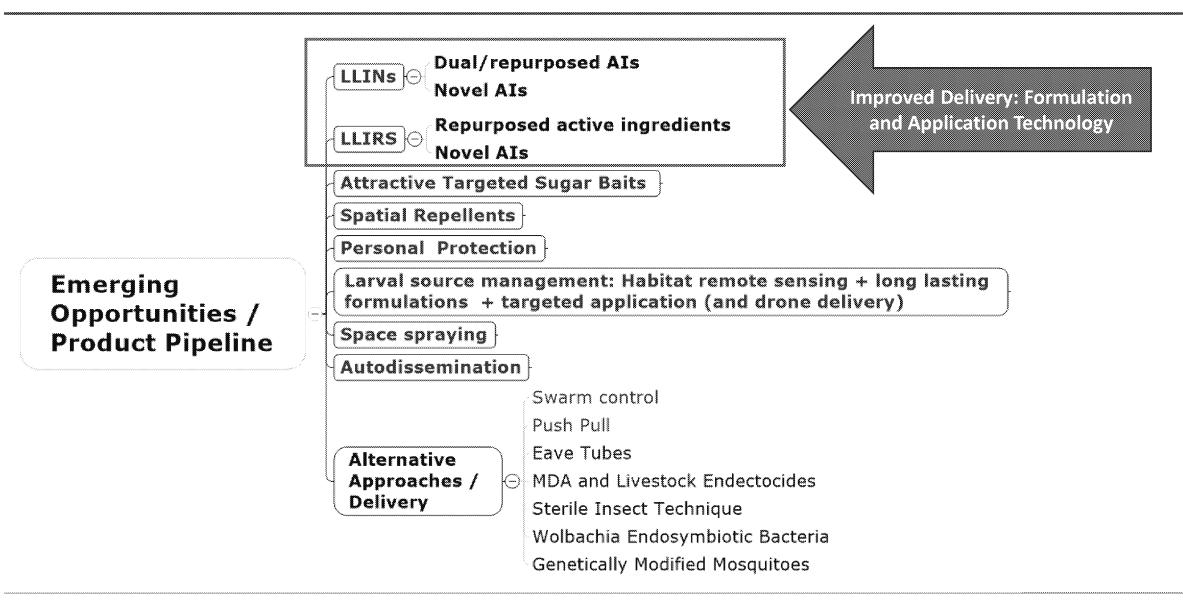
## Exploration of vector-control technologies is a rich area of research IVCC is actively working on areas outlined in red.





### IVCC and partner focus



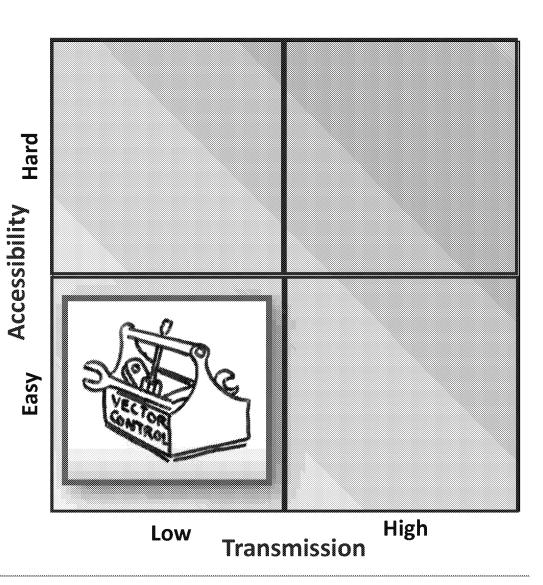


# Maintain the Gains....the start.... On track through repurposing



				Expected launch																	
ID	Project	Product	Status	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
3	K-Othrine Polyzone	LLIRS																			
12	Actellic CS	LLIRS																			
37	SumiShield	LLIRS																			
10	Interceptor G2	LLIN																			
41	Fludoro Fusion	LLIRS																			
	AI + PPF	LLIN																			
91	PBO LLINS	LLIN												000000000	************						

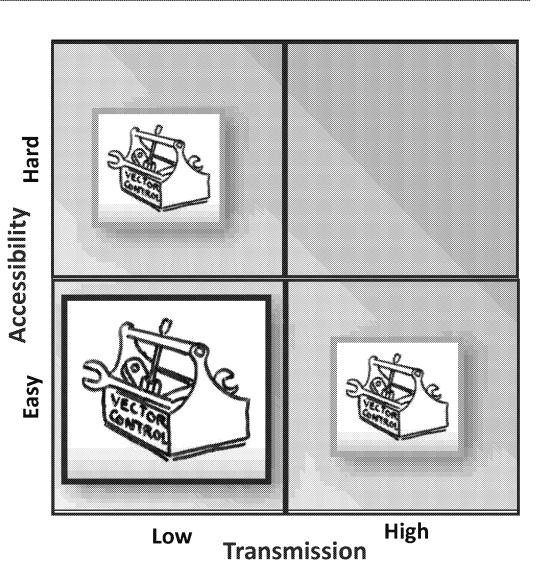




# Maintain the gains/reverse the trend Repurposed chemistry and new tools



			Expected launch																		
ID	Project	Product	Status	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
3	K-Othrine Polyzone	LLIRS																			
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41	Fludoro Fusion	LLIRS							***************************************												
	AI + PPF	LLIN																			
91	PBO LLINS	LLIN																			
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26		LLIN (impregnated)																			
26		LLIN (in mixture)							0000												
26		XLLIRS																			
71	T-Net	Trapping net																			
42	ATSB	ATSB outdoor																			



# Eradication Repurposed, Novel chemistry and transformational tools



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37	SumiShield	LLIRS																		10000000		I avayaya Ya				
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	AI + PPF	LLIN																		_						
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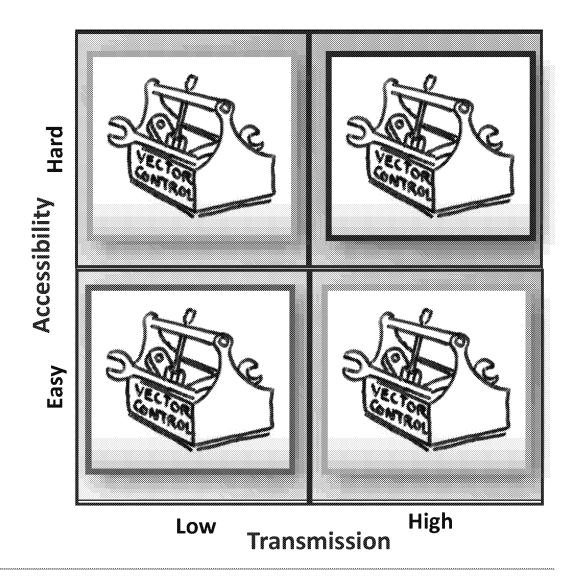
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Building Partnerships • Creating Solutions • Saving Lives

## Managing high transmission in poorly accessible regions



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ID	Project	Product	Status	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
3	K-Othrine Polyzone	LURS					····				*****		*******	*****							
12	Actellic CS	LLIRS																			
37	SumiShield	LLIRS																			
10	Interceptor G2	LUN																			
41	Fludoro Fusion	LLIRS																			
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91	PBO LLINS	LUN																			
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40	ED Sprayer	Improved sprayer																			8
66	CDA Sprayer	Improved sprayer																			000
93	VectoWeb	Surveillance																			000
Х	Chromobacterium	Adulticide																			
92	RNAi larvicide	Larvicide																			0000
	Aerial Larvicides	Disruptive tech.																			
	Aerial ATSB	Disruptive tech.																			
	Wolbachia	Disruptive tech.																			000
	Gene Drive	Disruptive tech.																			000
	Oxited	Disruptive tech.																			000

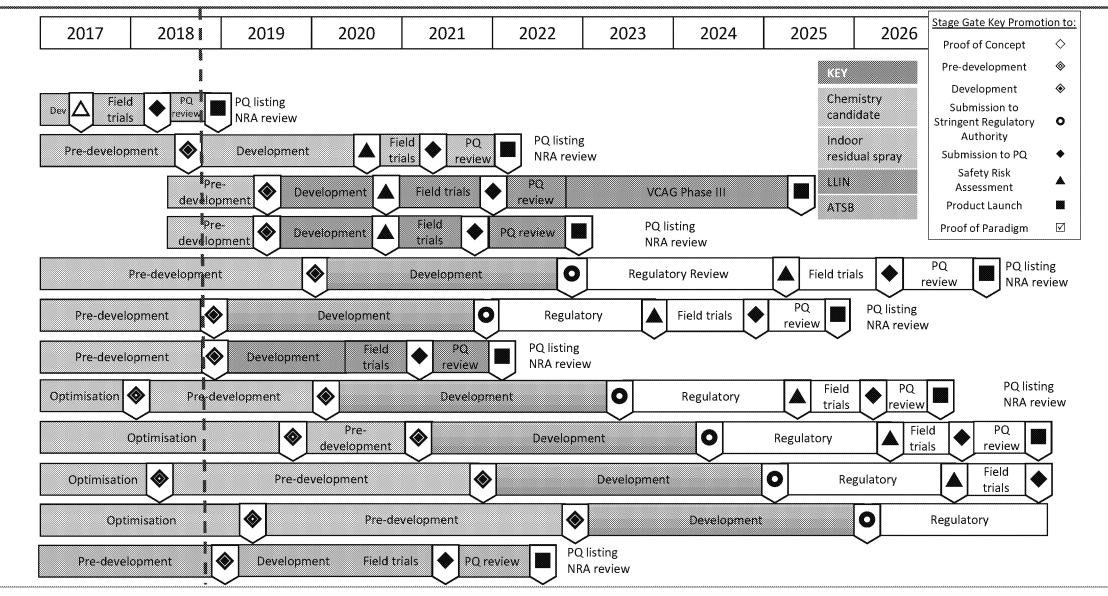


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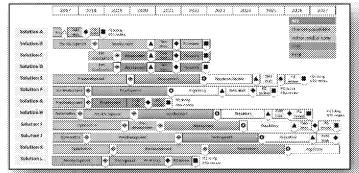
### Project timelines and additional technologies





# Building the Eradication Toolbox

Novel Active Ingredients
Repurposed Chemistry
Existing Tools and Technologies



Autodessimination

MDA Endectocides

Livestock Endectocides

Sterile insect technique

Wolbachia Endosymbiotic Bacteria
Genetically Modified Mosquitoes

Eave Tubes

Space spraying

Spatial Repellents

Personal Protection

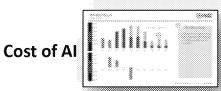




Mode of Action



Formulation and Efficacy



Flexibility



Toxicology



Probability of Success



#### **Toolbox of Interventions**



**IRM Rationale** 



Integrated Vector Management



Cost of intervention



Timeline

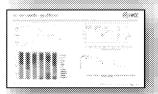
Regulatory

and



Market Access

**Approval** 



High Transmission Higher impact Lowest probability



Eradicate



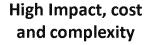
Eliminate



Maintain the gains

Lower Transmission Lower impact Highest probability

## Integrated Tools Management: Informed by Surveillance and modelling Smart Targeted Treatment vs. Universal Coverage..... (horses for courses!)













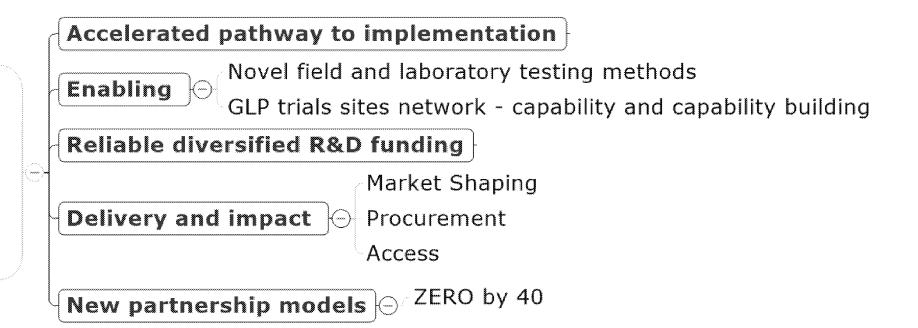


Lower impact, cost and complexity





Innovation must go beyond products alone



### Innovation must go beyond products alone

### A pragmatic approval process that partners with innovators



Accelerated pathway to implementation

Reshaping public health regulatory pathways

Global policy to realign with both the programmatic needs and biological realities of malaria vector control Creative methods to assess 'public health value' that reduce time to launch and cost

Δ

Novel field and laboratory testing methods

Age grading and species detection Surrogate markers - bridging between different classes of chamistry

Evaluating non-pyrethroid chemistry

GLP trials sites network - capability and capability building

Reliable diversified R&D funding \@ Creative funding models

Market Shaping

NgønIRS / UNITAID in tiativø New Nets Project (UNITAID)

Delivery and impact

Procurement — New Nets Project (Global Fund Catalytic Funding)

Arress - Global Access Plan

New partnership models

Sharing of IP and know-how to solve some of ZERO by 40 - the major challenges in vector control

## WHO Prequalification Team: Vector Control Products

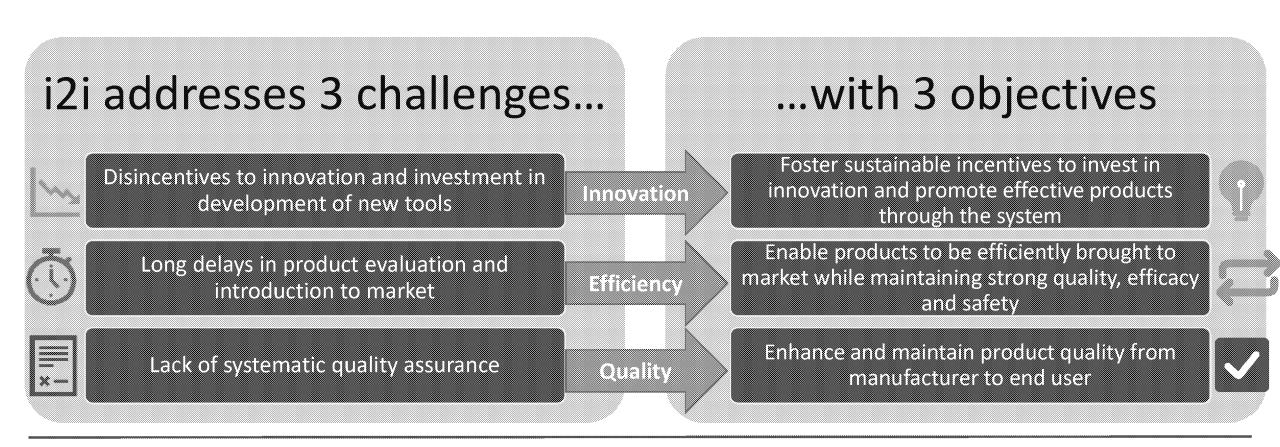


Vector control interventions have contributed substantially to controlling and eliminating vector-borne diseases. The 2015 World Malaria Report estimated that 663 million malaria cases had been prevented since 2001 with recent studies showing 69 per cent of cases averted were due to the use of mosquito nets, and a further ten per cent due to indoor spraying. The use of vector control products has also been critical in preventing the transmission of other major vector-borne diseases such as dengue fever, Chikungunya, Zika virus disease, Chagas disease, lymphatic filariasis, visceral leishmaniasis, and human African trypanosomiasis. If control and elimination targets for malaria and other vector-borne neglected tropical diseases are to be met over the 2020-2030 period, vector control interventions need to play an increasingly prominent role.

## What is Innovation to Impact (i2i)?



i2i is an initiative which aims to reduce the time to market of new vector control tools



### Sources of Suitable Chemistry Are Drying Up





Industry consolidation...

1982 1993 1994 1998 1998 1999 2000 2001 2002

Syndents

Syndents

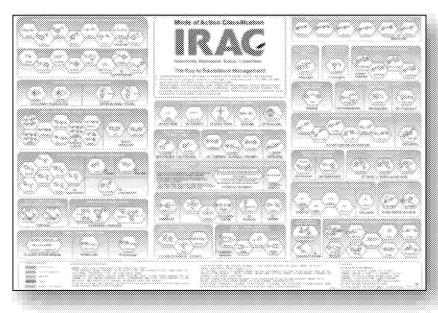
Average

Innovation, product development and market access historically comes from the agrochemical industry as repurposed insecticides

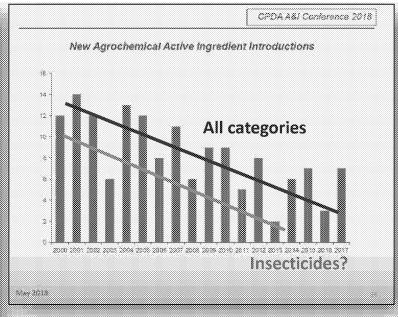
Rapidly declining numbers of insecticide R&D Based manufacturers

## Repurposed insecticides; is there much left to mine?





**Tetromic acid 23** METIZ1A . Sprayable Bt 11 EcR agonists 18 00000 Ottown Acytoreas 15 Carbamates 1A Diamides 28 Piprotes 28 VOSC blockers NTX analogs 14 Cordotonal Org. 5 Avermectins Spinosyns S Neonicationids Fig. 5. Distribution of total insecticide sales (percent of total value) by IRAC MoA Group or Subgroup. Total value + \$17,016 million; excludes funsigants, Based on 2013



Sparks and Nauen, 2014, Pesticide Biochemistry and Physiology 121 (2015) 122–128

Limited number of insecticide chemical classes available for repurposing

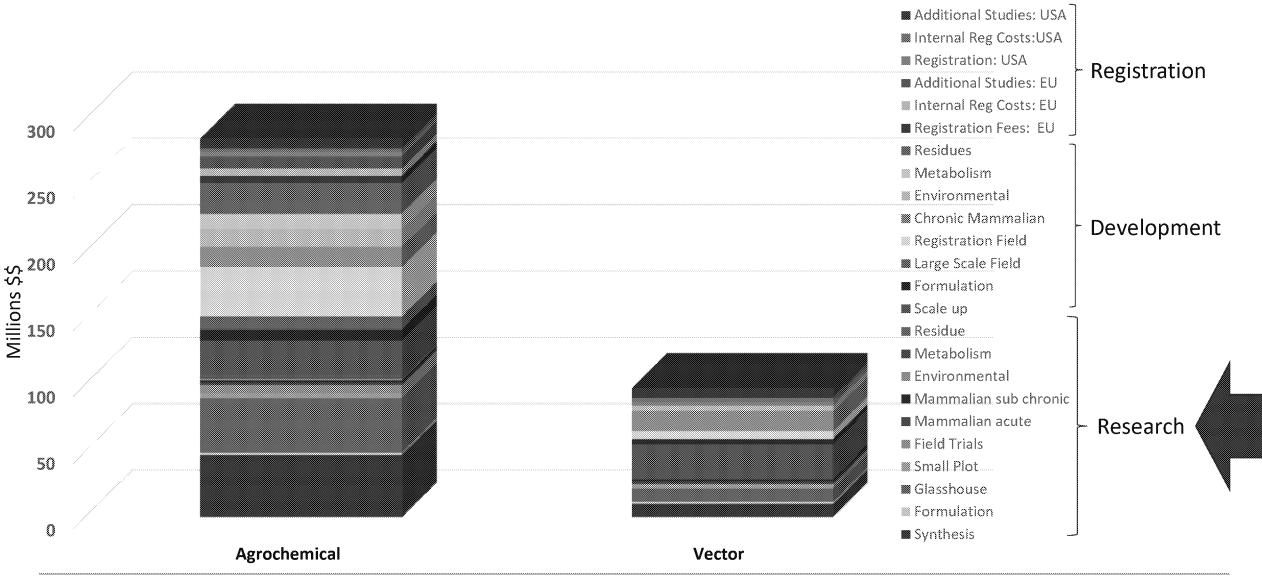
Completed review and testing of all registered insecticide modes of action for their potential in vector control.

End-user sales data from Acranova (24), July 2014.

Low expectations of future pipeline for vector control

## Development Costs for Novel Active Ingredients: It is Expensive and Complex

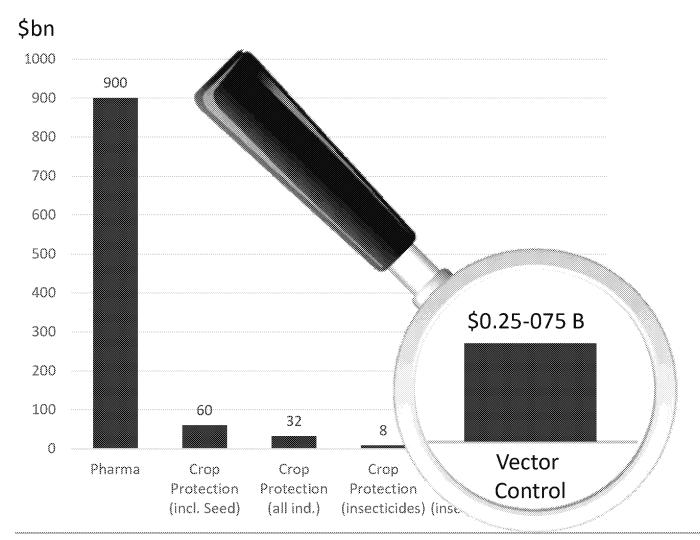




### Vector Control, Market and Innovation: a market failure...



### Small an unattractive market...



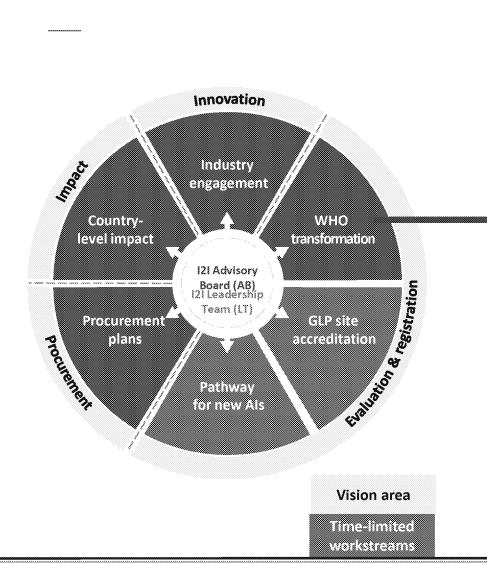


'Vector control is not seen as an attractive target for investment in R&D by private industry—the sector is regarded as relatively small, high risk and price driven with low barriers to entry leading to returns on investment that are insignificant or non-existent'

### Focus on: WHO Transformation







#### **WHO Transformation Workstream**

- Transition from WHOPES to new product evaluation system under WHO PQ is a key component of the i2i programme
- Initiated to address issues with WHOPES system: combined regulatory and policy functions; lack of predictability and transparency; inconsistent data quality; lack of systematic quality management
- PQ Pathway established for products within an existing product class. New Product Pathway established for products without a product class
- i2i role has been to facilitate engagement between WHO and the various stakeholder groups during the transition from WHOPES to PQ

### WHO Transformation Summary





### Key Activities:

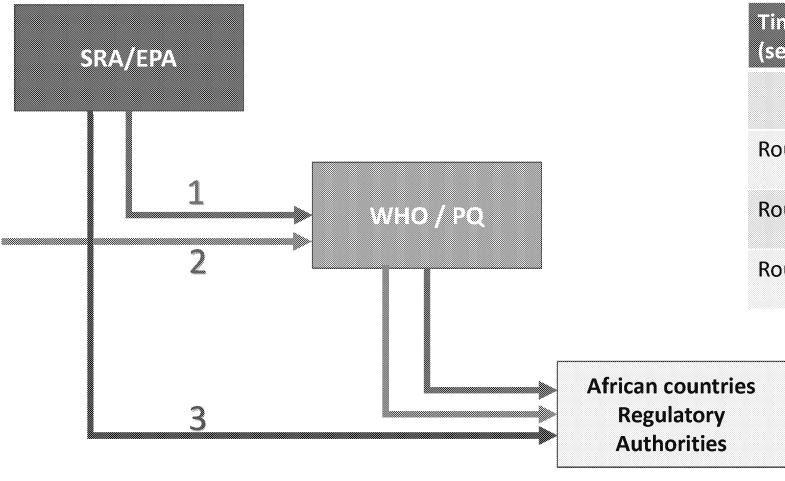
- PQ team established and 'doors open' from January 2017- WHOPES ceases to exist
- Team fully recruited (save for Entomologist post)- January 2018
- All WHOPES recommended products transitioned to a PQ listing (where requested by manufacturers)- May 2018

### **Next Steps:**

- Address remaining issues in the PQ system:
  - Data requirements for Phase III testing
  - Data protection for 'first in class' manufacturers
  - Transition to sole use of GLP sites
- Finalise roles and responsibilities between PQ and GMP regarding novel products
- Communicating the change in system to member states. Workshops planned with WHO RSS in Qs 1 and 2 2019: i2i is supporting PQ with this

# Regulatory routes: new routes seem possible, but how to have them work together?





## Time (months) for Regulatory Review (see notes for calculation)

	EPA	WHO	NRA	Total
Route 1	18	8	0	26
Route 2	0	12	0	12
Route 3	18		?	18+?*

#### **Assumptions:**

EPA expedited timeline is 18 months
WHO PQ review of novel a.i. is 12 months \*
WHO PQ of compound new to VC is 8 months
WHO PQ review of a.i. known to VC is 4 months

<sup>\*</sup> Valid for existing paradigms noting that efficacy data required by WHO could be 3-5 years

### Innovation must go beyond products alone

### A way to pay for innovation

II. 3 IVCC activities and New projects



Accelerated pathway to implementation

Reshaping public health regulatory pathways

Global policy to realign with both the programmatic needs and biological realities of malaria vector control Creative methods to assess 'public health value'

that reduce time to launch and cost

## DU A

Age grading and species detection

Surragate markers - bridging between different classes of chemistry

Evaluating non-pyrethroid chemistry

GLP trials sites network - capability and capability building



**Creative funding models** 

Market Shaping

testing methods

Novel field and laboratory

NgenIRS / UNITAID in tiative
New Nets Project (UNITAID)

Delivery and Impact

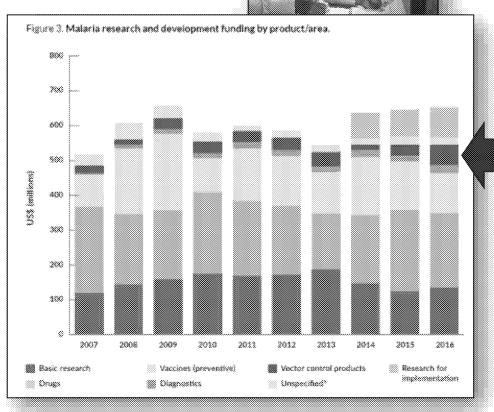
Procurement – New Nets Project (Global Fund Catalytic Funding)

Arress - Global Access Plant

New partnership

Sharing of IP and know-how to solve some of ZERO by 40 - the major challenges in vector control





### Agenda



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III. EPA Challenges and needs (EPA) (30 min)
Health security approach at local and global level

Break

IV. Incentivize innovation in Vector Control product regulatory pathways (IVCC and consultants) (30 min)

V. Debate and Next steps (All) (50 min)

VI. Conclusion (10 min)

### Driving innovation by rewarding market access of new life-saving vector control products



Novel and repurposed insecticides to reduce the Global Burden of Vector-borne Diseases

#### 

By David B. Ridley, Joffrey L. Moe, and Nat. Phono-

#### ANALYSIS & COMMENTARY A Voucher System To Speed Review Could Promote A New

Generation Of Insecticides To Fight Vector-Borne Diseases

800, 0 (0010) 1660 - 1666 40000 0 (0010) 1660 - 1

contents. Many in the scientific community are concerned about the potential increase in prevalence of insect-borne discuss such as Chagas disease, Chikungunya, dengue lever, malaria, and Zika in the United States and around the world. Sepond vaccines and drugs to prevent and treat these discuses, a comprehensive approach to lighting these discuses should include control of disease carrying vectors, such as mosquitoes. Vertor-control methods, such as using insecticales to treat hed nots and spray the walls of bosses, have prevented sollions of deaths from malaria. However, mosquitoes are becoming resistant to insectivides, and no new class of insectivides for vestor control has been introduced in decades. We recommend the excettion of a new type of incentive for the development and commercialization of safe new insecticides: a Vector Fundited Review Voucher, to be awarded to a sponsor that introduces a named inscribing for public health use. The rougher could be redeemed to expedite registration of a second, more profitable, product by the US Environmental Protection Agency.

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United States and around the world time to glidy constact, muchods, because insactivate resistant atacine and global climate drange. The a disconnections service, reproduce, and materily cases are abready within practice many consumer. I passing our resistance genes to their officiality, For example, maker's is potential to have billed. Purcharmon, no now clies of investigate active 4198 deep economic in 1988.

processing and training industries discusses, years. The Renthed commonded potential of has dury un insulficient." A comprehensive up— montinuos scales provides ministrana financial proach to lighting defection division would be a transfer for commercial research and devel-Circle mining the community health workers: opinion, above the development and communities and communities. assectativing rations, theheding mangaines, theheation of rate new inserticides, which are None, State, and they and the house reads. Yes - larger the conview of the US Emissions of the

actor/home Bareson, with an Chie - transmissional books, and at inactividacy of test gas disease. Colleangerpa, danigue - bed new and to apray the wells of blomes, have lesse, makeris, sexualissionissis, yel-perbased melecial transmission and presented low force. Whe Nike view, and Piles - millions of deaths of standards, account because analytic come programment open the code one reduced the effectiveness of contraingredienes has been decidened for long-booking Vaccions and design are interesting their for a magnetic had not produced to meet their fact.

ACCESSOR DOOR SHOW CONTRACTOR OF \$461

## Gov't options to overcome the VC market failure\*



To stimulate new public health pesticides (re-purposed existing or new AI's):

- Tax credits to cover costs of development
- Create or improve technical standards to evaluate products
- Create a prize or expand existing awards (e.g. VERV, data exclusivity extension)
- Provide budget support to expand agency capability
- Create a new market (VERV can be traded or sold)
- Benefits far outweigh costs
  - new fees cover agency burden
  - Potential gains to payer > costs

# Eligibility to incentives provided via an EPA assessment: a combination of cases to look at



What?	What class?	Where used?	Which product?		
		I- Used in the US	A- New Al specific for Vector control use		
Vector Control products	<ul><li>IRS</li><li>BedNets</li><li>ATSB</li><li>Larvicide</li><li>Others</li></ul>	II- Military Use III- Not used in the US (Public Health)	<ul> <li>B- New AI possible use for Ag and Vector control</li> <li>C- Already registered AI <ul> <li>a-Product with already registered AI never used in VC</li> <li>b- Product with already registered AI used in VC but in another class</li> <li>c- Product with already registered AI used in this class but in a different AI combination</li> </ul> </li> </ul>		



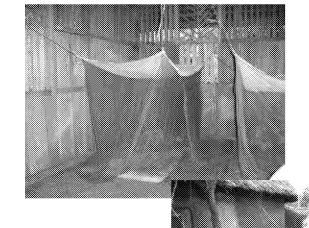
# Could EPA provide a technical assessment for products to be used only outside of the US? This could help and ease further assessment (like Article 58 within EMA)?

# Opening the number of products assessed by EPA: how to position it in regards of WHO PQ, which is not a regulatory approval?



#### Use categories

- Insecticide-treated nets
- Indoor residual sprays
- Mosquito larvicides
- Personal protection
- Space spray products
- Aircraft disinsection
- Molluscicide
- Rodenticide
- Sugar baits, ovitraps, Wolbachia, RNA and other biotechnologies



- The WHO has no experience in reviewing novel insecticide active ingredient dossiers
- NMCPs need to be convinced that EPA approved public health insecticides meet or exceed the established WHO global safety standards
- EPA needs to establish its brand credentials with Global Procurers who traditionally only purchase WHO approved products

WHO Use Categories PRIA categories	Insecticide -treated nets	Indoor residual sprays	Mosquito larvicides	Personal protection	Space spray products	Aircraft disinsec-tion	Molluscicide	Rodenticide	Other; ATSB, ovitraps, Wolbachia, RNA and other biotechnologi es
New Active (R060 or R110)	<b>✓</b>	✓	<b>4</b>	<b>✓</b>	<b>✓</b>	✓	<b>✓</b>	<b>✓</b>	1
New Use (indoor non-food) (R260)	✓	✓		skin applied, clothing, spatial repellent,	✓	✓		✓	
New Use (Outdoor non-food) (R230)			✓	<b>√</b> Spatial repellent	✓		✓	<b>✓</b>	✓
New Physical Form (R320)	✓	<b>√</b> (wall lining)	✓	✓		✓		✓	✓
New Product for existing use (R310)	•	Possibl e	<b>✓</b>	<b>✓</b>	•			•	Possible for ovitraps
New Product - New Exposure R350		✓						<b>✓</b>	
Fast-track/me-too (non-PRIA)	1		✓	1	1			1	
Section 18 (Non-PRIA)					✓	✓		<b>√</b>	00193801-00040

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# PRIA Public Health Use Category: new AI and added use to existing?

Multiple PRIA Public Health Use Categories?

#### Incentives: Allocated differently according to type of product



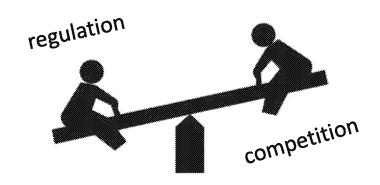
What incentive?	Who could it be granted to?	For which type of product?
_	Al manufacturer	A- New AI specific for Vector control use
Data Protection		<b>B</b> - New AI possible use for Ag and Vector control
	Final Product manufacturer?	C- Already registered AI containing products Under conditions to be defined
VERV		
		8 New All possible use for Agland Vector control

#### Intellectual Property or CBI Uncertainty





who unclear on intellectual property protection for new vector control Al's and new product classes

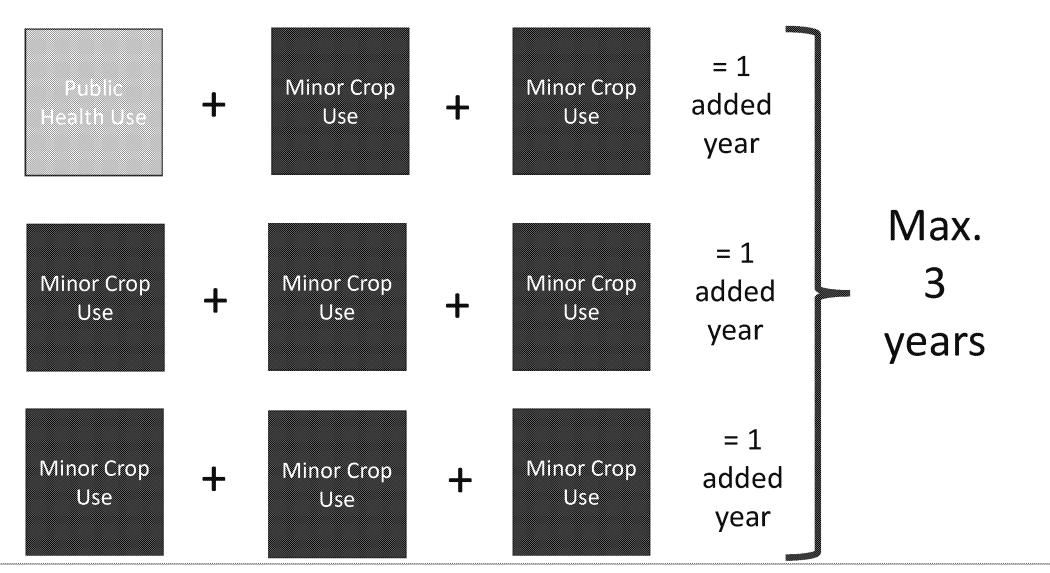


Data that defines a new product class must be sufficiently broad and robust to allow others to bring competitive products to a reliable, expeditious regulatory process: balance incentives to reward the class opener while promoting competition



#### Exclusive Use Extension Provision





#### Incentives: Allocated differently according to type of product



What incentive?	Who could it be granted to?	For which type of product?
		A - New All specific for Vertor control use
Protection		C-Aiready registered Al containing products Under conditions to be defined
VERV	Al manufacturer	<b>A</b> - New Al specific for Vector control use
V LIV	Patent owner / IVCC	<b>B</b> - New AI possible use for Ag and Vector control

#### Innovation must go beyond products alone

Vector Expedited Review Voucher (VERV)...a PRV for vector control.



Reshaping public health regulatory pathways

needs and biological realities of malaria vector control

Creative methods to assess 'public health value' that reduce time to launch and cost

Novel field and laboratory testing methods

GLP trials sites network - capability and capability building

#### Reliable diversified R&D funding (Creative funding models



#### 

Sty Control S. Kraffers, Joffrey L. More, and Nick Horse

#### ANALYSIS & COMMENTARY

A Voucher System To Speed Review Could Promote A New Generation Of Insecticides To Fight Vector-Borne Diseases

115 (165). Many in the scientific community are concerned about the potential increase in prevalence of insect-borne discusses such as Chaga discuss, Chikungunya, dengas fever, makeria, and Zika in the United States and around the world. Beyond vaccines and drugs to prevent and treat these diseases, a comprehensive approach to lighting these diseases. should include control of disease carrying vectors, such as marquitaes. Vector control methods, such as using insecticides to treat bed nets and spray the walls of homes, have prevented millions of deaths from malaria. However, mosquitoes are becoming resistant to inserticides, and no new class of insecticules for year or control has been introduced in decades. We recommend the creation of a new type of incentive for the development and commercialization of sale new insecticides: a Vector Expedited Review Voucher, to be awarded to a spensor that introduces a novel insecticide for public health use. The voucher could be redeemed to expedite registration of a second, more profitable, product by the US Environmental Protection Agency.

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Vaccines and drugs the important trace for a intentified had not manner in more than boty prompting and making telepropering discourse, years. The limited memorical percential of but they are insufficient. A memoricanity are according to the finite percential tensor fiction for the control of the control mounts or Burbins and class of the constructed in the construction of the construction close training for continuous health workers; opinion. placation for communities; and commit of the accomming veters, including acceptations, distinguished of one insectionly, which are

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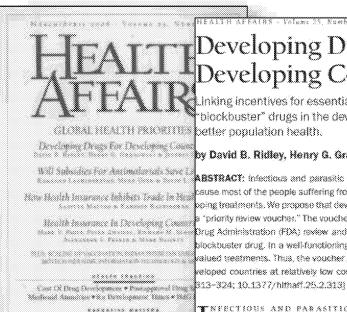
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#### Priority Review Voucher (2008 FDA program) overcomes NTD market failure by rewarding new Tx





Name of Property Company (Sec. 1981)

\*\*\*\*\*\*\*

#### Developing Drugs For Developing Countries

inking incentives for essential drugs in developing countries with blockbuster" drugs in the developed world would help both achieve better copulation health.

by David B. Ridley, Henry G. Grabowski, and Jeffrey L. Moe

ABSTRACT: Infectious and parasitic diseases create endomous health burdens, but beause most of the people suffering from these diseases are poor, little is invested in devel pping treatments. We propose that developers of treatments for neglected discuses receive "priority review voucher." The voucher could save an average of one year of U.S. Food and Drug Administration (FDA) review and be sold by the developer to the manufacturer of a pockbuster drug. In a well-functioning market, the voucher would speed access to highli valued treatments. Thus, the voucher could benefit consumers in both developing and de reloped countries at relatively low cost to the taxpayer. [Health Affairs 25, no. 2 (2006)

rnfectious and parasitic dispases accounted for more than half of healthy years lost in Africa in 2002, but only 3 percent of healthy years lost in Ldeveloped countries. Communicable diseases that disproportionately affect becople in developing countries include malaria, leishmaniasis. Chagas disease, tu berculosis, dengue fever, and African trypanosomiasis. Lack of scientific knowl edge is not the major harrier to drug development for many of these diseases. Sei ntists know more about the biology, immunology, and genetics of leishmania and rypanosomes than any other parasites.3 Rather, successful compounds often do not enter costly clinical development. The barrier is a lack of financial incentive. Secause most people suffering from these neglected diseases live in low-income countries, there is little financial incentive for private pharmaceutical companies to invest in research and development (R&II) for new treatments."

We propose a "priority-review vougher" as an incentive to drug companies to develop therapies for neglected diseases. To receive a voucher, a therapy must meet the following criteria: (1) treat neglected diseases such as African trypanosomiasis, Chagus discase, leishmaniasis, or dengue fever; (2) receive approval by the

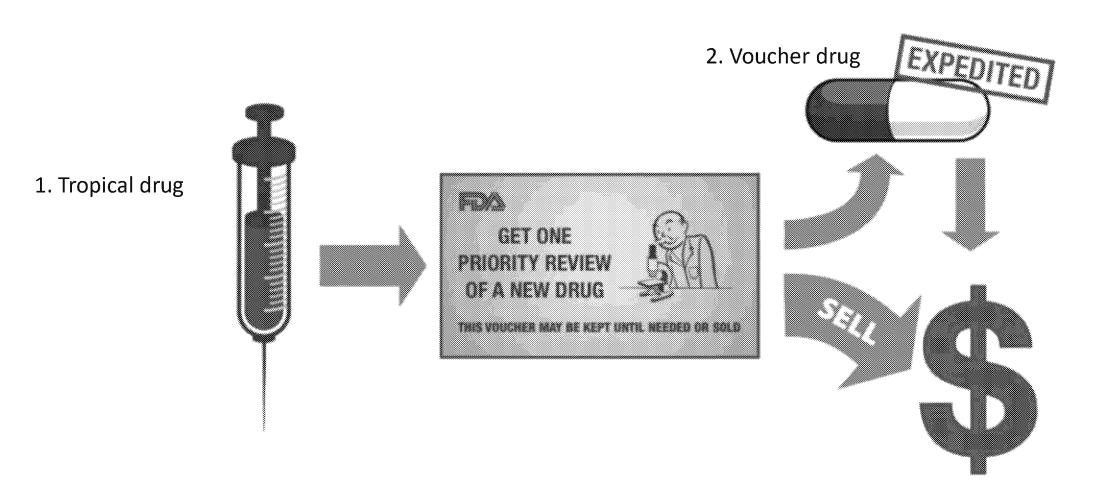




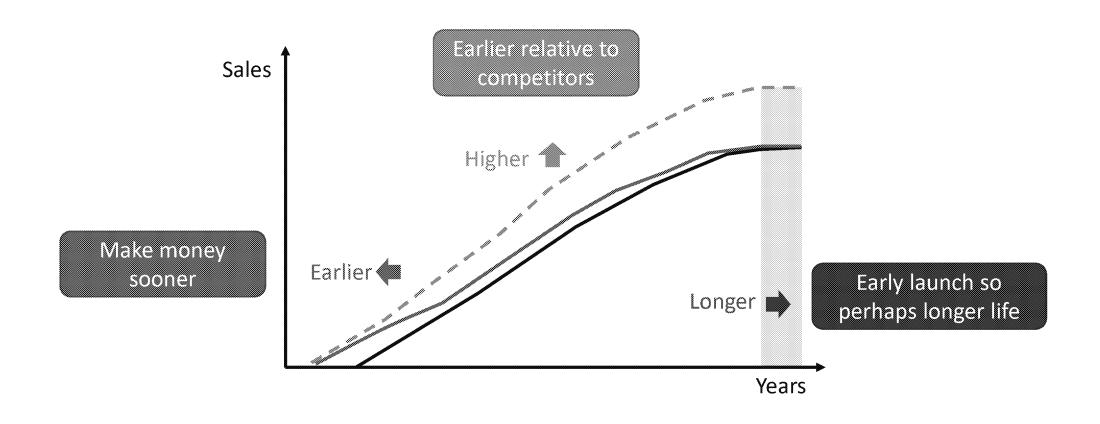


Henry Grabowski Duke **Economics** 









#### Eligible NTD Diseases – can be amended

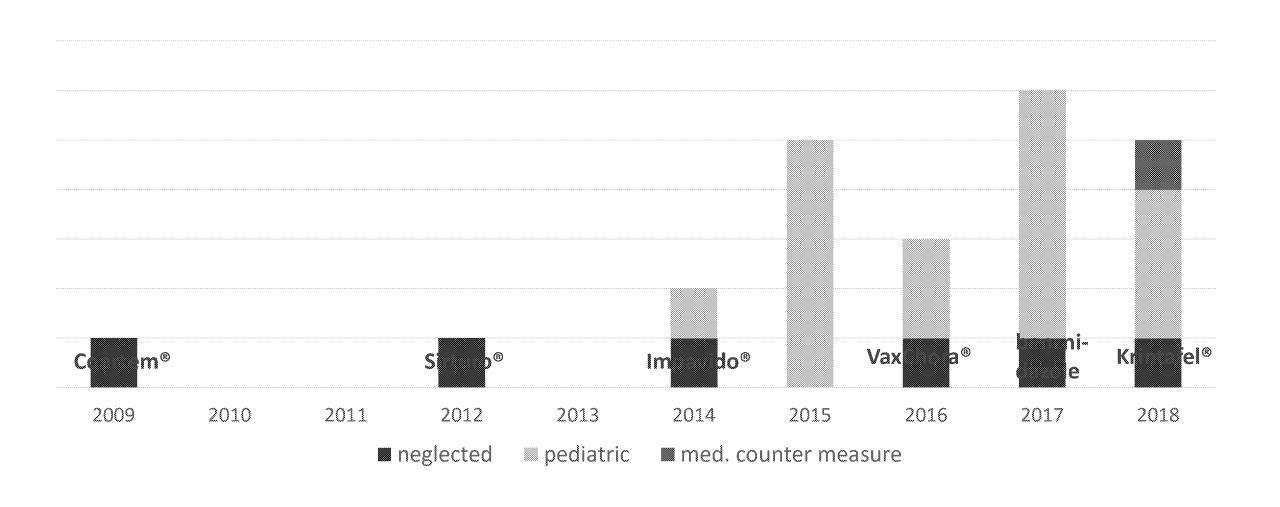


- Blinding trachoma
- Buruli Ulcer
- Chagas (FDA 2015)
- Cholera
- Chikungunya Virus Disease (2018)
- Dengue
- Dracunculiasis
- Fascioliasis
- Filoviruses (Ebola) (Cong. 2014)
- Human African trypanosomiasis
- Lassa Fever (2018)
- Leishmaniasis
- Leprosy

- Lymphatic filariasis
- Malaria
- Medical countermeasures (Congress 2016)
- Meningitis, Cryptococcal (2018)
- Neurocysticercosis (FDA 2015)
- Onchocerciasis
- Rabies (2018)
- Rare pediatric (Congress 2012)
- Schistosomiasis
- Soil transmitted helminthiasis
- Tuberculosis
- Yaws
- Zika (Congress 2016)

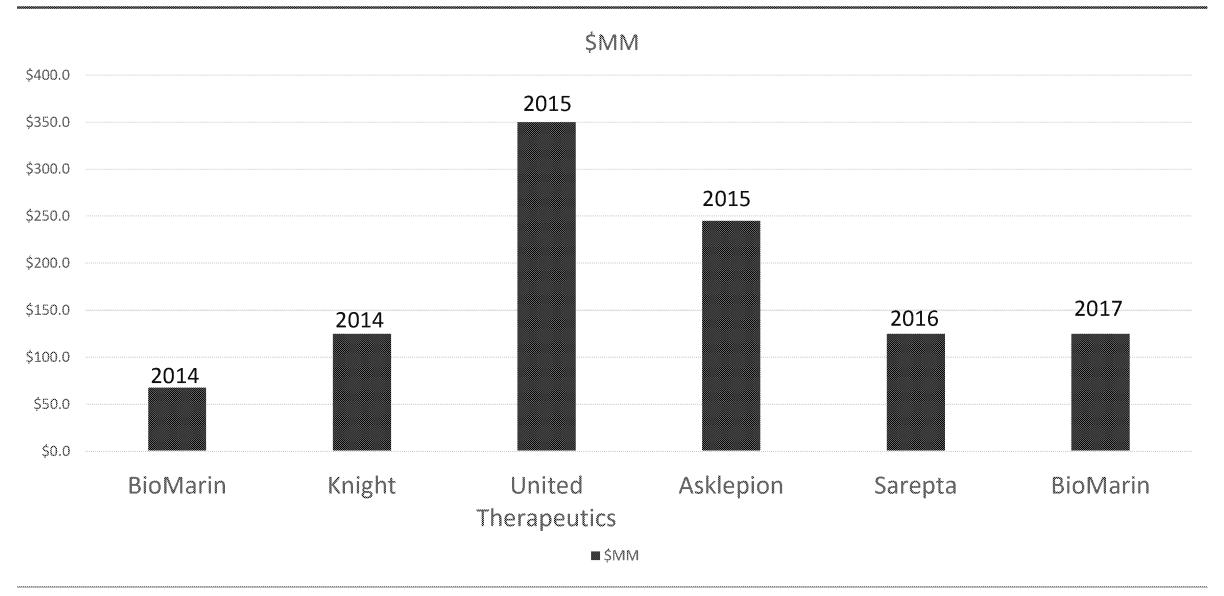
#### 23 Priority Review Vouchers Awarded





#### Sales of Vouchers





<sup>\*</sup> Wellstat sold voucher in 2015 for undisclosed amount

#### **Vector Expedited Review Voucher:**

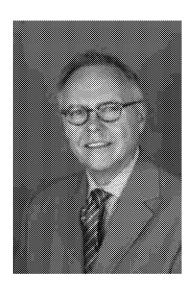
A mechanism to foster innovation in public health







Pavid B. Ridley
Fuqua
School of Business
Duke University



Jeffrey L. Moe

Duke
Global Health Institute



Nick Hamon
Innovative
Vector Control
Consortium

#### VERV proposed mechanism

(emulates the FDA Priority Review Voucher)



#### Screening criteria:

- Novel insecticide active ingredient (i.e. not already registered by EPA or other stringent regulatory authorities)
- Meet EPA data requirements
- Target a neglected public health vector (list to be established by EPA, CDC, WHO)

#### Review package:

- Complete EPA data package
- Global access plan (to be updated every 3 years)
- IRM strategy
- Monitoring plan

Expedited review <u>does not</u> lower safety review (PRIA)

GOOD FOR ONE

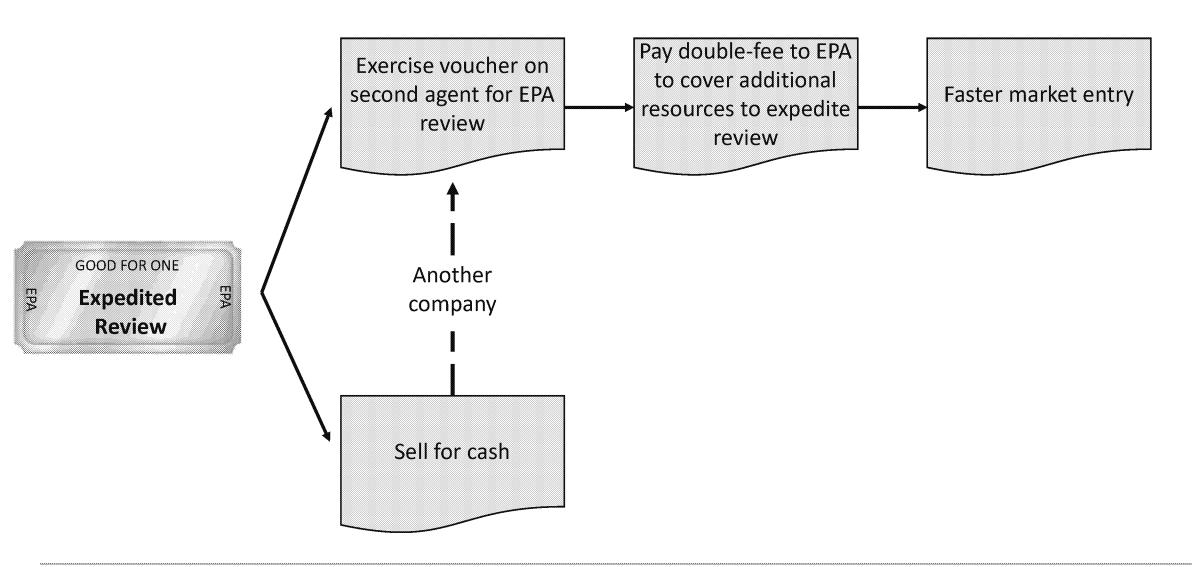
Expedited

Review

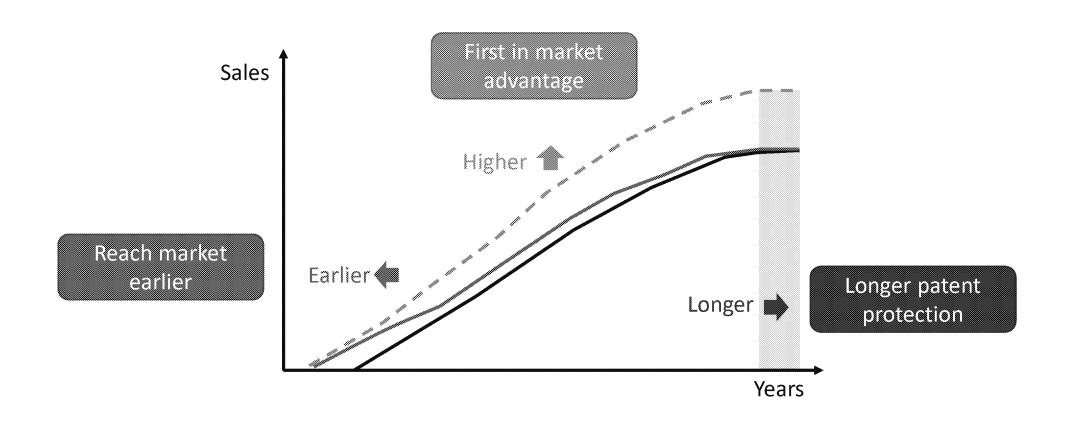
#### VERV proposed mechanism

(inspired from PRV)









#### Estimated voucher value

(based on annual sales, by PRIA dossier review category and timeline for conventional pesticides)



	Change in review	Estimated voucher value (\$ millions) based on initial annual sales (\$ millions) of:			
PRIA* dossier review category	Current PRIA time (months)	Proposed voucher time (months)	\$100	\$200	\$400
New active ingredient, food use	24	18	\$38	\$77	\$153
New active ingredient, food use, reduced risk	18	12	39	78	156
New active ingredient, non-food use; outdoor	21	15	39	77	155
New active ingredient, non-food use; outdoor, reduced risk	16	12	25	51	102
New active ingredient, non-food use; indoor	20	14	39	78	155
New active ingredient, non-food use; indoor; reduced risk	14	12	12	25	50

<sup>\*</sup> NOTE: PRIA times have not been established; legislation pending

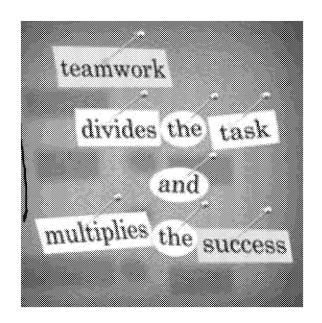
#### Potential issues to be managed



Potential risks	Mitigation proposed		
'Windfall profits' (VERV awarded for products developed but not previously submitted to EPA)	Manufacturer plan if windfall profits occur		
Products may not be marketed	Global Access Plan (GAP); update every 3 years		
Burden on EPA	Double fees cover expedited review costs		
EPA does not meet VERV expedited review times	Monitor VERV implementation		
EPA registration too costly & less attractive than WHO Pre-qualification or other stringent regulatory authority	Harmonize EPA with WHO PQ process		



- Create a Task force with some internal EPA resource?
- Can we identify priorities? Low hanging fruits?

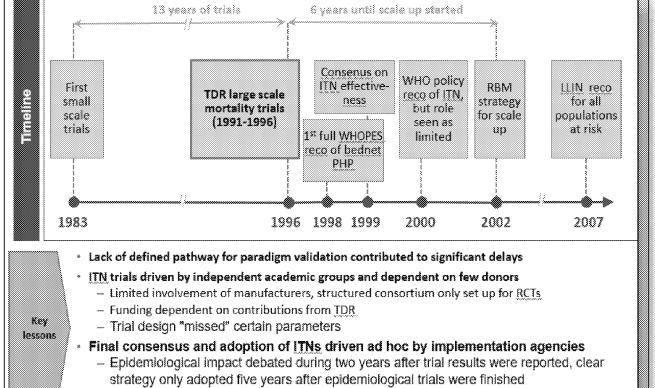


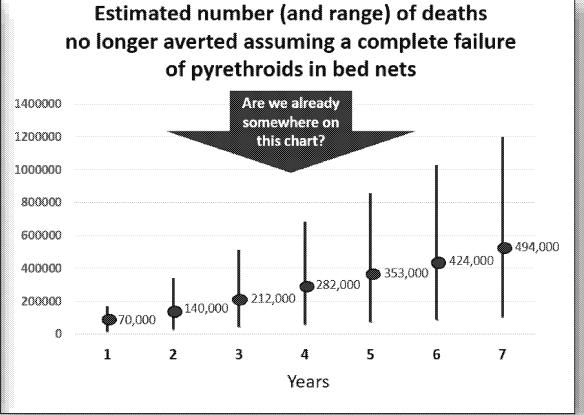
### We must use the right metrics to measure impact and take the appropriate level of risk?



ITN development took 19 years from start to scale up Approximately ~1 million lives at stake each year in the late 1990's

People treated or people impacted?





#### Innovation must go beyond products alone

#### A complete rethink of what partnership and collaboration means?



Accelerated pathway to implementation

a Enabling (G

Reshaping public health regulatory pathways

Global policy to realign with both the programmatic needs and biological realities of malaria vector control

Creative methods to assess 'public health value' that reduce time to launch and cost

P450 Assays

Novel field and laboratory

Age grading and species detections are species detections.

Surrogate markers - bridging between different classes of chemistry

Evaluating non-pyrethroid chemistry

GLP trials sites network - capability and capability building

Reliable diversified RRD funding (G) Creative funding models

Market Shaping

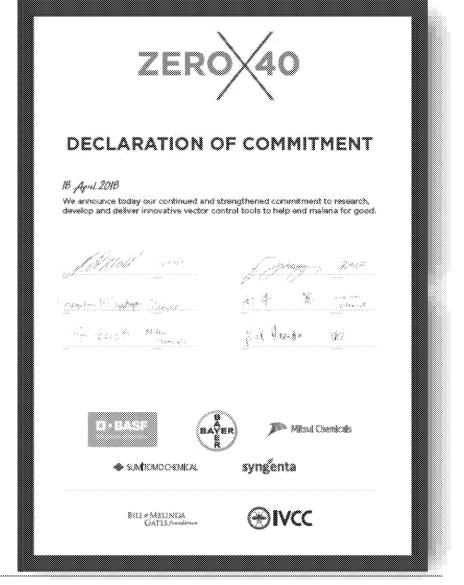
testing methods

NgenIRS / UNITAID in tlative
New Nets Project (UNITAID)

procurement - New Nets Project (Global Fund Catalytic Funding)

Arres - Global Access Plan

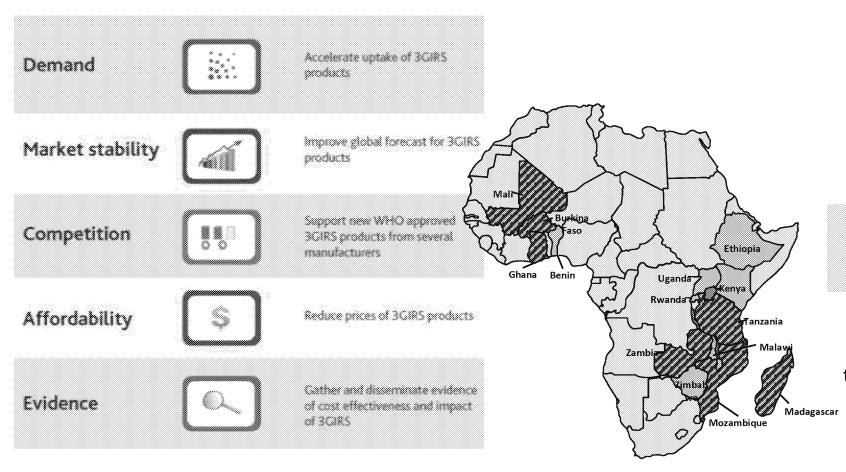
New partnership models Sharing of IP and know-how to solve some of ZERO by 40 The major challenges in vector control



#### Impact: Novel interventions are already saving lives (direct)



Market-shaping intervention to support PMI (leader IRS), GFRs & other implementation partners expand coverage with 3GIRS







It is estimated that NgenIRS supported IRS campaigns in 12 countries in 2017 averted between 960k and 1.9m cases of malaria and between 1.820m & 3,640 deaths, mostly children.

20 – 40% drop in prevalence reported in NgenIRS countries where Actellic® 300CS impact evidence is being collected.

Estimated number of

people protected

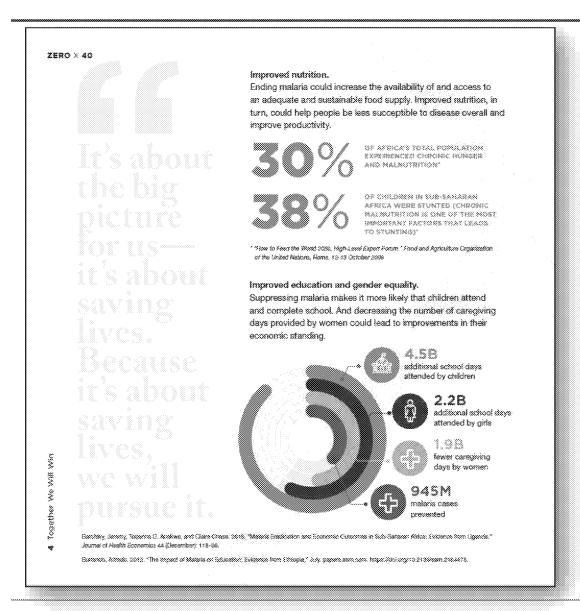
throughout Africa with 3GIRS insecticides since

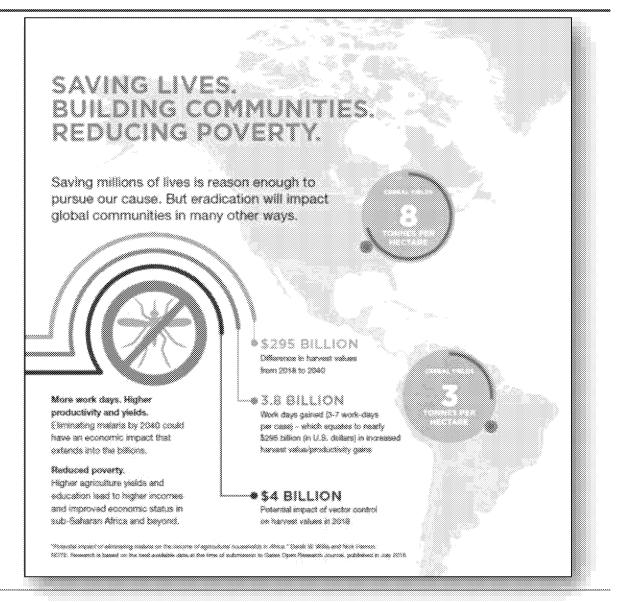
2016 is

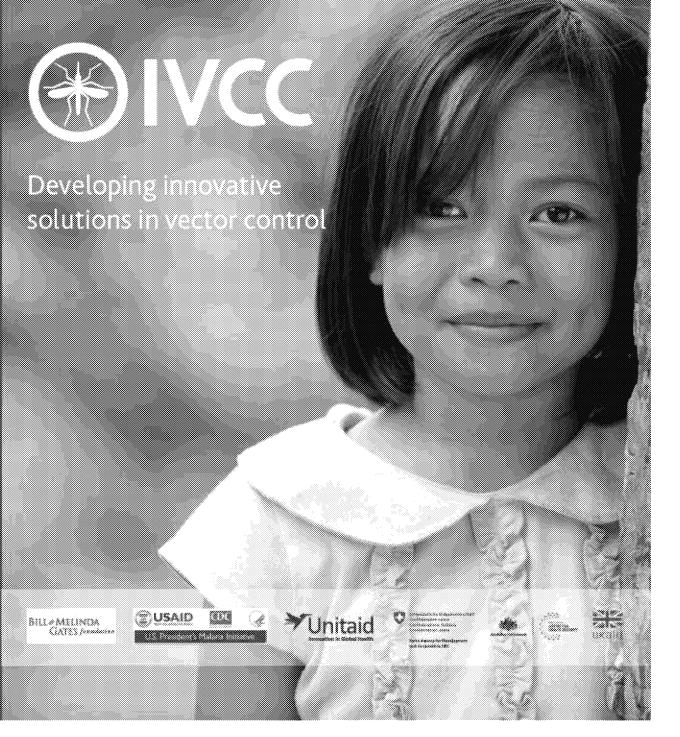
81 million.

#### Impact: Novel interventions are already saving lives (Indirect)









Thank you for your time and attention

